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PSYCHOBIOLOGY OF SUICIDE BEHAVIOUR*

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SUMMARY

Evidence from genetic research, monoamine studies and psychopharmacological trials points towards a possible biological predisposition and precipitant for suicidal behaviour. The implications for early detection and management based on a biological model have been discussed. The limitations of the model have been discussed.

Psychoanalytically suicide is an inwardly directed aggression against an internalized object. (Freud 1917). Ringel (1976) postulates a 'presuicidal syndrome', a form of a chronic neurosis that predisposes to suicide and whose features comprise constriction of affect, values and social relations, a reversal of aggression and suicide phantasies. Feelings of guilt, ideas of hopelessness and helplessness have been found to be strong potentials for suicide. (Beck et al 1985). Mental illness especially Affective Disorder of depressive type, personality disorder and schizophrenia also eventuate in suicide in some cases. There are clinical predictors of suicide risk within the symptom constellation of depressive illness. The intensity of depression used to be judged by patient's expression of suicidal thoughts and the suicide attempt. However, a lack of clear correlation between the thoughts and the attempt on the one hand and the severity of depression on the other is being recognised. The superiority of Montgomery and Asberg's (1979) scale over the conventional HRSD has been demonstrated in detecting this anomaly.

During the last over two decades, the monoamine theory of affective illness has been having its sway and naturally biological accompaniments of suicide behaviour became the focus of research. Consequently a biological construct of suicide behaviour is being worked out. There are still many gaps. Such a formulation however does not negate the importance of psychological and social factors involved in suicide behaviour. This presentation offers certain psychobiological facets of suicide behaviour extracted from the available literature at present.

Genetic Studies

Though the occurrence of suicidal deaths in families has been noted over the years, cultural and psychological attributes shared by the members were considered significant overlooking the genetic role. In 1947, Franz Kallman could not observe any concordance for suicide in his classic work on twins, although he found high concordance for schizophrenia and manic depressive illness in MZ twins (Kety, 1985). Twenty years later, in a meta-analysis of many studies, Haberlandt found 18% concordance rate for suicide

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among the monozygotic twins (Kety 1985). In 1970, Juel-Nielsen found a significant concordance rate in monozygotic twin pairs dying through suicide (Kety 1985). In a study using the National Health Registry data of the Danish citizens, Schulsinger identified 57 adoptees born between 1925-48 who had committed suicide by the late 1960's. Victims' family histories revealed the incidence of suicide among biological relations to be 4.5% in contrast to an incidence of less than 1% among the biological relations of a matched controlled group. There were no suicides among the adopted relatives of either group. (Kety 1985). An investigation by Kety revealed 19 suicides among all relatives of the adoptees of whom 15 were by biological parents, siblings and half siblings of the depressed adoptees. The highest incidence of suicide was noted among the biological relatives of those suicides in whom the diagnosis of affective disorder was made. The current studies though not indicative of an exclusive genetic determinism of suicide behaviour, enable one to conclude that "among people who have a life experience that could lead to suicide, only those with the genetic predisposition will actually do so" (Kety 1985). Kety (1985) has summarised the contemporary research on the genetics of suicide behaviour. There are other reports that tend to confirm these findings (Venkoba Rao et al 1987 under publication).

Endocrines and Neurotransmitters

More than two decades age, Bunney et al (1965) demonstrated an increased urinary excretion of cortisol metabolites in the depressed suicidal subjects. Bunney and Fawcet (1965) observed a high risk for suicide in those with an elevated plasma cortisol and urinary steroids. They attributed this risk to an increased 'emotional turmoil' in the patients. Currently, this is explained on the basis of the changes in the hypothalmic pituitary adreno-cortex axis (Sachar 1976; Carroll et al 1976). Though there is an increased cortisol in the depressives, there are no clinical features of hypercorticalism. Cushing Syndrome is occasionally complicated by suicide, especially the hypothalmic type in which psychiatric manifestations are common. There are reports on Dexamethasone Suppression Test in suicide attempters. In a series of 17 patients who made suicide attempts, 14 were found to be the non-suppressors' in contrast to 9 out of 32 depressive patients, who had not made suicide attempts. It is not clear whether non-suppression is specific for the diagnosis of depression or the psychological state in which people commit suicide (Targum 1985). Those DST non-suppressors on clinical improvement, failing to convert to suppressors fared badly in terms of relapses or suicide behaviour. In these cases relapses or repetition of suicide attempts were found to be common (Coryell and Schlesser 1981). Carroll et al. (1981) advocate that DST is to be done 48 hours following suicide attempts. Regarding the question as to how long it would take for DST to be normal following the suicide attempt, it depends upon the nature of the stress that prompted the attempt. There are reports of suicide following serial DST. For instance, 3 completed suicide have occured next morning following dexamethasone test (Targum 1985). Suicide figures as an important terminator of myxoedema.

Amine hypothesis explains the affective disorders of mania and depression on the basis of elevated or decreased levels of indoleamines and/or catecholamines in the central synaptic sites. It is the functional balance between these biogenic amines rather than their absolute excess or deficiency that is of pertinence. A low level of 5HIAA in the cerebrospinal fluid in the

depressives especially indulging in violent forms of suicidal behaviour has ben a consistent finding in a number of well designed studies (Asberg et al 1976; Traskman et al 1981, Asberg and Traskman 1979). Low levels of serotonin have been reported in the hind brains on autopsy on suicidees in a project by the Medical Research Council of Great Britain (Shaw et al 1967) and of 5HIAA from the NIMH, Bethesda (Bourne et al, 1968). Lloyd et al. (1974) in a study of discrete brain areas found that serotonin levels were reduced significantly in the raphe nuclei dorsalis and centralis inferior. They also studied higher brain stem and telencephalon, where they found normal concentrations of serotonin but possibly increased 5 HIAA in the mamillary bodies. Bourne et al (1968) found no abnormality in hypothalmic and hind brain NE or in caudate dopamine concentrations. The associated occurrence of the low levels homovanillic acid, the metabolite of dopamine in CSF of the depressed suicidal probands was reported by Asberg and Traskman (1979) and Montgomery and Montgomery (1983).

Serotonin deficiency is known to be associated with diverse forms of aggressive behaviour. In depression, aggression turned inwards results in suicide. It is also not uncommon to find depressives display aggression externally. The potential suicide is known to entertain death wishes against others. Murderous acts preceding suicide in the depressives are not uncommon (Rosenbaum 1983). That a large number of suicide attempters have been destructive towards others has been commented upon by Shafii (1986). Brown and his co-workers (1979) reported on the low CSF 5 HIAA in the military personnel with 'hostile outbursts'. A significant relationship was found between Rorschach protocols on aggressive drives and low CSF 5 HIAA (Rydin et al quoted by Asberg and Traskman, 1979). A decrease turnover of serotonin in certain types of aggressive behaviour in animals has been reviewed by Eichelman (1979) and Delini-Stula and Vassout (1979).

Lapin and Oxenkrug (1969) and Curzon (1972) have hypothesised that elevated cortisol levels cause a decrease in serotonin synthesis by diminishing the availability of tryptophan through its action on tryptophanpyrrolase. Alternatively, monoamines may be involved in the control of the corticotropin releasing factor too (Weiner and Ganong 1978). The correlation between lowered 5 HIAA and high suicide rates has been noted in 20% of all the patients studied. At present, the conclusion on the relationship is "a lot of people with low serotonin do not kill themselves, but none with high levels did". (Goodwin 1985). It is not yet clear whether a low serotonin is an indicator of severity of depression, or suicide behaviour or aggression.

Buchsbaum et al (1976) observed an increased incidence of suicide behaviour in the relatives of the probands with a low platelet MAO activity. Such a relation was also noticed in the psychiatrically ill patients by Buchsbaum et al (1977). Gottfries et al (1980) reported on the alcoholics who died from suicide showing low MAO activity have been reported by Schooler et al (1978) in the normal, non case persons. These included suicidal behaviour and other anti-social activities. It is likely that MAO activity and cortisol secretion are related to serotonin turn-over. A low platlet MAO may serve as a predictor of suicide risk in the depressed subjects.

A low melatonin syndrome of depression has been documented by Beck-Friis (1983) and Wetterberg et al (1981). Friis' patients ran a lower risk for suicide.

Venkoba Rao et al (1984) reported on the depressives with differing levels of urinary melatonin and their association with suicidal behaviour. With antidepressant therapy, and with the clinical improvement the melatonin levels reverted to normal. The failure to return to normal denoted a tendency to relapse. The low melatonin may reflect the low serotonin turnover since serotonin is the precursor of melatonin and it may also indicate a low noradrenergic tone. The difference between these reports in respect of suicide risk with low melatonin has been commented upon by Venkoba Rao (1986).

Seasonality in the occurrence of suicide has been reported, its peaks occurring in late spring and early summer (Kevan 1980; Aschoff 1981). Such regular variation has been observed in mental hospital admissions, use of ECT and other psychiatric therapies in affective disorders. Circannual rhythms of pineal function in animals have been observed and a seasonal alteration in the weights of the pineal in the humans on autopsy have been recorded (Wetterberg 1978). Beck-Feriis et al (1984) reported on the seasonal variation in melatonin secretion in man. There is thus a close parallel between neuroendocrinological changes and monoamine metabolites on the one hand and suicide behaviour on the other. However not all depressives display a low 5 HIAA profile. In many others, the levels are normal or even elevated. This highlights the heterogenous nature of clinical depression.

Nondepressive suicide behaviour

Suicide is not to be equated with depressive illness, though earlier researchers emphasised depression and alcoholism as twin major contributors to suicide. There are, doubtless, causes other than these. Personality disorder is equally important among those who attempt or complete suicide (Venkoba Rao 1986; Kreitman 1977; Shaffer 1986). In Shaffer's series, cases of personality disorders outnumbered the depressives (DSM III category). The problems were antisocial and of conduct, and the use of drugs with the attempts being invariably impulsive.

A significant reduction of 5 HIAA in the CSF was observed in many suicide cases in the absence of depression, alcoholism, Schizophrenia and Organic syndromes. In many of these instances, psychopathology failed to conform to the conventional psychiatric diagnostic categories. Thus a low CSF 5 HIAA seems to link itself with suicide behaviour, irrespective of the underlying diagnosis. Interestingly Montgomery and Montgomery (1983) have pointed to possible low HVA levels in the nondepressive suicide attempters bringing them on par with the depressive suicides. They drew upon the beneficial effect from drugs which elevated dopamine in these cases though the CSF did not reveal such deficit. Further work is called for in this area.

Measures to elevate monoamine levels

Prevention of suicide is a complex affair and it is difficult to accomplish this in any appreciable way – especially its primary prevention. During recent years pharmacoprophylaxis of suicide has been possible. Treatment of suicide behaviour in depression calls for treatment of depression itself. Lithium and tricyclics have proved useful as long term prophylactics against suicide (Venkoba Rao et al 1982; Barraclough 1972; Prien 1979). Lithium nonresponders are known to be susceptible to carbamazepine (Grof 1983). In view of the low 5 HIAA and HVA in the CSF of especially the depressives and of 5 HIAA in nondepressive suicides, newer strategies aiming at elevating them are available.

Zimelidine, a bicyclic antidepressant is a powerful inhibitor of uptake of serotonin (Coppen et al 1979). It has proved superior to amitriptyline in raising the 5 HIAA levels in the earlier stages of treatment of the depressed suicidal patients (Montgometry et al 1981). This is the antidepressent of choice when a quick effect is desirable.

Management of suicide behaviour in personality disorder in fraught with difficulties owing to non-cooperation, hostility and non-compliance factors. The comparative superiority of flupenthixol over mianserin and placebo in these cases has been reported by Montgomery, Roy and Montogmery (1981). Flupenthixol's action is mediated through dopamine without involving 5 HIAA. Although there was no demonstrable change in CSF HVA levels in non-depressive suicidals, these authors speculate such an abnormality from the observed benefits from flupenthixol. This opens up a new field of pharmacotherapy in suicide behaviours of the personality disordered individuals.

Suicide is a well-recognised dreaded complication of depression on responsive to conventional antidepressant drugs. Failure of the levels of CSF monoamines to rise by pharmacotherapy is noticed in these patients. ECT has been used on such non-responders to tricyclics and MAOI, with dramatic effects resulting in elevation of CSF monoamine metabolites (NIMH 1985 personal communication). The use of ECT in cases of acute depression with suicide risk is established and needs no repetition. Thus newer measures to elevate the monoamine metabolite include Zimelidine and Flupenthixol. The oldest method of treatment – ECT – is now shown to do this in some refractory cases of depression. It is to be cautioned that to elevate serotonin level is not the aim in suicide prevention. The exact role of serotonin in psychiatric illness awaits clarification.

Newer Approaches

Psychiatric research in recent years has shifted its focus towards the 'high risk' groups from the 'already ill' persons. Recognition of 'Subaffective disorder' as forerunner of syndromal affective disorder is an instance of such approach (Akiskal 1981). Modern genetic research and understanding the monoamine metabolism in suicidal individuals, depressed as well as nondepressed, has given important leads to recognising the 'high risk' suicide prone individuals though a small group. A lower 5 HIAA, HVA, melatonin levels and platalet MAO are likely to serve as traits (markers) that would enable identification of suicide proneness and institution of appropriate treatment. Individuals with these traits are likely to react with suicidal behaviour under the impact of stressful situation. To detect them will be a formidable undertaking on a large population.

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